Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	3022	Cell (graft OR implant)	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 11:00
L2	885	mullerian inhibiting substance	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 11:00
L3	51	l1 and L2	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 11:02
L4	2	("5759830").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/09/02 11:09
L5	3	(("6068837") or ("5645829")).PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/09/02 11:09
S1	29	Donahoe patricia	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/01 17:25
S2	885	mullerian inhibiting substance	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 10:44
S3	12910	cell matrix	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/01 17:26
S4	157	S2 and S3	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/01 17:26
S5	29	mullerian inhibiting substance.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 10:49
S6	1	S5 and gene therapy	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 10:51
S7	885	mullerian inhibiting substance	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 10:51
S8	419	S7 and gene therapy	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/09/02 10:51

S9	376	S8 and (matrix polymer)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/02 10:52
S10	37	S8 and (matrix polymer).clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/02 10:53
S11	133	S9 and (graft implant)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/09/02 10:56

```
=> d his

     (FILE 'HOME' ENTERED AT 11:19:46 ON 02 SEP 2005)

     FILE 'MEDLINE, CANCERLIT, AGRICOLA, CAPLUS, SCISEARCH' ENTERED AT
     11:20:07 ON 02 SEP 2005
L2          1660 S MULLERIAN INHIBITING?
L3             8 S L2 AND (GENE THERAPY)
L4             8 DUP REM L3 (0 DUPLICATES REMOVED)
L5        294145 S CELL (L) (TRANSPLANT? OR IMPLANT?)
L6            30 S L2 (L) L5
L7            13 DUP REM L6 (17 DUPLICATES REMOVED)
L8            13 SORT L7 PY
L9       1089271 S MATRIX OR SCAFFOLD OR HYDROGEL? OR BIOAMATRI?
L10           23 S L2 (L) L9
L11           15 DUP REM L10 (8 DUPLICATES REMOVED)
L12           15 SORT L11 PY
                 E DONAHOE PATRICIA?/AU
L13          184 S E2
                 E MACLAUGHLIN DAVID?/AU
L14           85 S E2
L15           89 S L13 AND L2
L16           43 S L14 AND L2
L17           95 S L16 OR L15
L18           81 DUP REM L17 (14 DUPLICATES REMOVED)
L19            4 S L18 AND L5
L20            2 S L18 AND L9
L21            4 S L19 OR L20
L22            4 DUP REM L21 (0 DUPLICATES REMOVED)

=> d an ti so au ab pi l22 1-4

L22  ANSWER 1 OF 4     MEDLINE on STN
AN   2002425819     MEDLINE
TI   Highly purified mullerian inhibiting substance
     inhibits human ovarian cancer in vivo.
SO   Clinical cancer research : an official journal of the American Association
     for Cancer Research, (2002 Aug) 8 (8) 2640-6.
     Journal code: 9502500. ISSN: 1078-0432.
AU   Stephen Antonia E; Pearsall Lisa A; Christian Benjamin P; Donahoe
     Patricia K; Vacanti Joseph P; MacLaughlin David T
AB   PURPOSE: Mullerian inhibiting substance (MIS) causes
     Mullerianduct regression in mammalian, avian, and reptilian embryos; MIS
     also inhibits growth in vitro of Mullerian-derived cell lines
     and primary cells from human ovarian carcinomas.  We hypothesize
     that highly purified MIS delivered parenterally inhibits ovarian cancer in
     vivo.  EXPERIMENTAL DESIGN: To test the efficacy of highly purified MIS
     against ovarian cancer cell lines in vivo, we treated
     immunosuppressed mice with MIS after implanting OVCAR 8 or IGROV
     1 human ovarian cancer cells beneath the renal capsules and
     measured tumor volume over time.  Animals were treated with daily
     injections of 10 micro g of purified exogenous recombinant human MIS or by
     endogenous MIS secreted from cells growing on biodegradable
     mesh.  RESULTS: The average graft size ratio (change in size compared with
     starting size) of the OVCAR 8 tumor implants was larger in the
     control animals than in animals treated for 2 weeks (P < 0.019) or 3 weeks
     (P < 0.001) with parenteral MIS, or after treating with MIS produced from
     transfected cells, which impregnated the biodegradable mesh (P =
     0.02).  The average graft size ratio of the IGROV 1 tumors was also larger
     in the control animals than in those treated with injected MIS (P =
     0.0174).  CONCLUSIONS: Highly purified recombinant human MIS, delivered
     parenterally, or MIS produced endogenously causes inhibition of human
     ovarian cancer cell lines in vivo, providing convincing
     preclinical evidence to support the use of MIS as a parenteral agent for
     the treatment of ovarian cancer.

L22  ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2001:565104  CAPLUS
DN   135:127275
```

TI Delivery of therapeutic biological from implantable tissue **matrices**

SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2

IN Vacanti, Joseph P.; **Donahoe, Patricia K.**; **MacLaughlin, David T.**; Masiakos, Peter T.

AB Normal **cells**, such as fibroblasts or other tissue or organ **cell** types, are genetically engineered to express biol. active, therapeutic agents, such as proteins that are normally produced in small amts., for example, MIS (**Mullerian inhibiting** substance), or other members of the TGF-beta family HerceptinTM, interferons, and anti-angiogenic factors. These **cells** are seeded into a **matrix** for **implantation** into the patient to be treated. **Cells** may also be engineered to include a lethal gene, so that **implanted cells** can be destroyed once treatment is completed. **Cells** can be **implanted** in a variety of different **matrixes**. In a preferred embodiment, these **matrixes** are **implantable** and biodegradable over a period of time equal to or less than the expected period of treatment, when **cells** engraft to form a functional tissue producing the desired biol. active agent. Ovarian cancer **cell** lines that were responsive to MIS in vitro were place beneath th renal capsules of mice. CHO B9 **cells** seeded onto a polyglycolic acid **matrix** and were **implanted** in the mice. MIS produced by th B9 **cells** significantly inhibited the growth of the human ovarian cancer **cell** line in vivo.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001055212	A2	20010802	WO 2001-US2694	20010126
WO 2001055212	A3	20020124		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

L22 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:222623 CAPLUS

DN 135:29396

TI Tissue-engineered cells producing complex recombinant proteins inhibit ovarian cancer in vivo

SO Proceedings of the National Academy of Sciences of the United States of America (2001), 98(6), 3214-3219
CODEN: PNASA6; ISSN: 0027-8424

AU Stephen, Antonia E.; Masiakos, Peter T.; Segev, Dorry L.; Vacanti, Joseph P.; **Donahoe, Patricia K.**; **MacLaughlin, David T.**

AB Techniques of tissue engineering and **cell** and mol. biol. were used to create a biodegradable **scaffold** for transfected **cells** to produce complex proteins. **Mullerian Inhibiting** Substance (MIS) causes regression of Mullerian ducts in the mammalian embryo. MIS also causes regression in vitro of ovarian tumor **cell** lines and primary **cells** from ovarian carcinomas, which derive from Mullerian structures. In a strategy to circumvent the complicated purification protocols for MIS, Chinese hamster ovary **cells** transfected with the human MIS gene were seeded onto biodegradable polymers of polyglycolic acid fibers and secretion of MIS confirmed. The polymer-**cell** graft was **implanted** into the right ovarian pedicle of severe combined immunodeficient mice. Serum MIS in the mice rose to supraphysiol. levels over time. One week after **implantation** of the polymer-**cell** graft, IGROV-1 human tumors were **implanted** under the renal capsule of the left kidney. Growth of the IGROV-1 tumors was significantly inhibited in the animals with a polymer-**cell** graft of MIS-producing **cells**, compared with controls. This novel MIS delivery system could have broader applications for other inhibitory agents not amenable to efficient purification and provides in vivo evidence for a role of MIS in the treatment

of ovarian cancer.

L22 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:144219 CAPLUS
DN 116:144219
TI Recombinant human **Mullerian inhibiting** substance inhibits human ocular melanoma cell lines in vitro and in vivo
SO Cancer Research (1992), 52(5), 1182-6
CODEN: CNREA8; ISSN: 0008-5472
AU Parry, Robert L.; Chin, Taiwai; Epstein, James; Hudson, Peter L.; Powell, David M.; **Donahoe, Patricia K.**
AB Since **Mullerian Inhibiting** Substance (MIS) causes regression of the Mullerian duct, the anlagen of the uterus, vagina, and fallopian tube, it was expected and previously observed that purified recombinant human MIS causes regression of gynecol. tumors. However, recent expts. indicating that neural crest derivs. might be responsive to MIS prompted study of a group of human ocular melanoma **cell** lines in 4 in vitro inhibition assays, and a subrenal capsule assay in vivo. Ocular melanoma **cell** lines that grew well in a resp. assay were studied with MIS to determine whether this biol. modifier could inhibit growth. Three human ocular melanomas, OM431, OM467, and OM482, were growth-inhibited by highly purified human recombinant MIS in soft agarose. A dose-dependent tumor inhibition was noted when OM431 **cells** were incubated with MIS in a liquid colony inhibition assay. In addition, OM467 was inhibited by MIS in a multicellular tumor spheroid assay. **Cell** cycle anal. indicated that OM431 **cells** were inhibited in monolayer by MIS while in G1. At 100-fold lower serum concns. than required in the media of in vitro assays, MIS delivered via i.p. osmotic pumps inhibited in vivo the growth of OM431 **implanted** beneath the renal capsule of nude and CD-1 irradiated mice when compared to mice given **implants** of pumps containing no MIS. The responsiveness of ocular melanoma to MIS broadens the spectrum of tumors that might be treated with MIS and suggests further investigation of other neural crest tumors.